

### REMARKS

Claims 2, 4, 12, 26-29, and 60 have been canceled without prejudice. Claims 1, 6, 13, 14, 15, and 59 have been amended. Support for the amendments can be found throughout the specification (e.g., page 3, lines 1-4 and 15-19; page 31, lines 18-20). No new matter has been introduced and no new issue has been raised. These amendments have been made solely to expedite allowance. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

#### Information Disclosure Statement

Applicants note that the Examiner has considered and initialed the Information Disclosure Statements filed on December 6, 2004 and March 14, 2005.

#### Election/Restriction

The Examiner has acknowledged Applicants' election, with traverse, of Group I (claims 1-29 and 59-60) and SEQ ID NO: 231 from Table 6 in the Response filed on January 23, 2006.

Applicants reiterate the arguments already made of record and respectfully traverse the sequence election requirement. In particular, Applicants remind the Examiner that the claimed invention relates to a *genus* of nucleic acid compounds that decrease the expression of EphB4 in a cell (e.g., antisense nucleic acids and siRNA constructs), rather than a *species* nucleic acid compound selected from the claimed genus. The independent *genus* claims (e.g., claims 1 and 59) do not recite any specific nucleic acid *species*. It is inappropriate for the Examiner to restrict the claimed invention to an un-recited *species* in a *genus* claim, because doing so amounts to using Restriction Requirement to limit the scope of independent claims that have not yet been examined on merits. Accordingly, Applicants respectfully request reconsideration and withdrawal of the election requirement.

Claim Objections

The Examiner has acknowledged that the claims 14-17 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and deleting non-elected subject matter.

In response, Applicants have amended independent claim 1 to include the subject matter of claims 2, 4, and 12 solely to expedite prosecution of this application. Claims 2, 4, and 12 have been canceled accordingly without prejudice. Similarly, Applicants have amended independent claim 59 to include the subject matter of claim 60 and canceled claim 60 accordingly without prejudice. However, Applicants reiterate that the independent *genus* claims (e.g., claims 1 and 59) do not recite any specific nucleic acid *species* and should not be limited to the subject matter of claim 14. Applicants respectfully request reconsideration and withdrawal of this objection.

Claim Rejections under 35 U.S.C. § 112, First Paragraph

Claim 9 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Specifically, the Office Action asserts that "[t]he specification as filed discloses antisense compounds targeted to EphB4 that inhibit expression as designated by a series of "+" symbols (see Table 8). The specification does not provide adequate written description of a nucleic acid compound targeted to a nucleic acid encoding EphB4 that inhibits expression of EphB4 by 50% or greater . . . there are no examples provided in the specification nor does the prior art provide a core structure or motif that would impart the function of inhibiting by at 50%." See Office Action, page 4, lines 8-15; page 5, lines 1-6.

Applicants respectfully traverse the Examiner's assertion and submit that the specification sufficiently describes the claimed invention. For example, the specification teaches that "[n]ucleic acid compounds may inhibit expression of the target by about 50%, 75%, 90% or more when contacted with cells under physiological conditions and at a concentration where a nonsense or sense control has little or no effect (e.g., page 3, lines 24-31; page 4, lines 1-2, emphasis added). Further, the specification provides at least four

examples of nucleic acid compounds (e.g., AS-8, AS-9, AS-10, AS-11) that inhibit EphB4 expression by at least 50% (see, e.g., Figure 43A).

Nonetheless, solely to expedite prosecution of the application, Applicants have canceled claim 9 without prejudice, rendering the rejection moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of all rejections for lack of written description.

Claim Rejections under 35 U.S.C. § 102(b) or § 103(a)

Claims 1-7, 9-13, and 59-60 are rejected under 35 U.S.C. § 102(b) or § 103(a) as allegedly being anticipated by Bennett et al. (US Patent No. 6,150,162). Applicants respectfully traverse the rejection to the extent it is maintained over the claims as amended.

Independent claim 1 as amended recites an isolated nucleic acid compound comprising at least a portion that is complementary to at least 15 contiguous nucleotides of an EphB4 transcript sequence set forth in SEQ ID NO: 392 and decreases the expression of EphB4 in a cell, wherein the nucleic acid compound is an antisense nucleic acid compound.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. “A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1978).

Applicants contend that Bennett et al. fail to satisfy the criteria for anticipating the present invention. Bennett et al. describe antisense compounds for modulating the expression of CD44. Bennett et al. do not teach or suggest antisense compounds for decreasing the expression of EphB4. More specifically, Bennett et al. fail to teach or suggest an antisense nucleic acid compound comprising at least a portion that is complementary to at least 15 contiguous nucleotides of an EphB4 transcript sequence set forth in SEQ ID NO: 392. Accordingly, Bennett et al. do not teach all the elements of independent claim 1 or 59 and fail to anticipate claims 1 and 59. For the same reasons, Applicants submit that all claims depending from claim 1 or 59 are not anticipated by Bennett et al.

Applicants further submit that Bennett et al. do not render obvious the instant claims. The instant claims relate to antisense nucleic acid compounds for decreasing the expression of EphB4, whereas Bennett et al. are concerned with modulation of the expression of CD44. Indeed, Bennett et al. are absolutely silent on EphB4 as a target for antisense compounds. In the absence of any suggestion in the cited art that the EphB4 gene expression should be targeted for inhibition, one of skill in the art would not have been motivated to make EphB4 antisense nucleic acids as claimed in this application.

Claims 1-13, 26-29, and 59-60 are further rejected under 35 U.S.C. § 102(b) or § 103(a) as allegedly being anticipated by Pavco et al. (US Patent No. 6,346,398). Applicants respectfully traverse the rejection to the extent it is maintained over the claims as amended.

Pavco et al. describe nucleic acid molecules for modulating the expression of vascular endothelial growth factor receptors. Pavco et al. do not teach or suggest antisense compounds for decreasing the expression of EphB4. More specifically, Pavco et al. fail to teach or suggest an antisense nucleic acid compound comprising at least a portion that is complementary to at least 15 contiguous nucleotides of an EphB4 transcript sequence set forth in SEQ ID NO: 392. Accordingly, Pavco et al. do not teach all the elements of independent claim 1 or 59 and fail to anticipate claims 1 and 59. For the same reasons, Applicants submit that all claims depending from claim 1 or 59 are not anticipated by Pavco et al.

Applicants further submit that Pavco et al. do not render obvious the instant claims. The instant claims relate to antisense nucleic acid compounds for decreasing the expression of EphB4, whereas Pavco et al. are concerned with modulation of the expression of vascular endothelial growth factor receptors. Indeed, Pavco et al. are absolutely silent on EphB4 as a target for antisense compounds. In the absence of any suggestion in the cited art that the EphB4 gene expression should be targeted for inhibition, one of skill in the art would not have been motivated to make EphB4 antisense nucleic acids as claimed in this application.

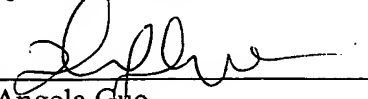
In sum, in view of the claim amendments and the arguments above, neither Bennett et al. nor Pavco et al. anticipate or render obvious the instant claims. Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) or § 103(a).

**CONCLUSION**

In view of the above remarks, Applicants believe that the pending application is in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. If an additional fee is due, please charge our Deposit Account No. 18-1945, under Order No. VASG-P01-001.

Dated: August 3, 2006

Respectfully submitted,

By   
Z. Angela Guo

Registration No.: 54,144  
ROPES & GRAY LLP  
One International Place  
Boston, Massachusetts 02110-2624  
(617) 951-7000  
(617) 951-7050 (Fax)  
Attorneys/Agents For Applicant